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(71) Applicant (*for all designated States except US*): **THE QUEEN'S UNIVERSITY OF BELFAST** [GB/GB];
University Road, Belfast BT7 1NN (GB).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **EARLE, Martyn, John** [GB/GB]; 40a Inishowen Drive, Finaghy, Belfast BT10 0EU (GB). **KATDARE, Suhas, Prabhakar** [IN/GB]; 27C University Street, Belfast BT7 1FY (GB).

(74) Agent: **MURGITROYD & COMPANY**; 373 Scotland Street, Glasgow G5 8QA (US).

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(54) Title: OXIDATION OF ALKYL-AROMATIC COMPOUNDS

(57) Abstract: A process for the oxidation of an alkyl-aromatic compound, wherein the aromatic compound is admixed with an oxidising agent or sulfur compound in the presence of an ionic liquid is described. In this process, air, dioxygen, peroxide, superoxide, any other form of active oxygen, nitrite, nitrate, nitric acid or other oxides (or oxyhalides) of nitrogen (hydrate or anhydrous) are preferably used as the oxidising agent. The process is usually under Bronsted acidic conditions. The product of the oxidation reaction is preferably a carboxylic acid or ketone or an intermediate compound in the oxidation such as an aldehyde, or alcohol. The oxidation is preferably performed in an ionic liquid containing an acid promoter such as methanesulfonic acid.

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10 Oxidation of alkyl-aromatic compounds
11

12 This invention relates to a process for the oxidation
13 of aromatic compounds such as toluene and xylene. The
14 oxidation of compounds such as toluene and xylene are
15 important reactions and are carried out on a large
16 scale. The products of the oxidation reactions, e.g.
17 terephthalic acid, are widely used in the polymer
18 industry.
19

20 Various methods exist for the oxidation of toluene,
21 including oxidation with dioxygen, using a
22 cobalt(III)^{1,2} catalyst, periodate,³ air using
23 $\text{Cs}_5[\text{SiW}_{11}\text{O}_{39}\text{Ru(III)(H}_2\text{O)}] \cdot 7 \text{ H}_2\text{O}$ as a catalyst (59%
24 yield),⁴ hypochlorite catalysed by Ru(VIII)oxide
25 tetroxide in $[\text{Bu}_4\text{N}]\text{Br}$.⁵ These methods work well, but
26 require either stoichiometric quantities of oxidising
27 agent or require special catalysts.
28

29 We have developed a procedure for the oxidation of²
30 alkylated aromatic compounds that either partially or
31 completely oxidises the alkyl group to an alcohol,
32 aldehyde, ketone or carboxylic acid.

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1
2 Thus, according to one aspect of the present invention,
3 there is provided a process for the oxidation of an
4 alkyl-aromatic compound, wherein the aromatic compound
5 is admixed with an oxidising agent or sulfur compound
6 in the presence of an ionic liquid.

7
8 In this process, air, dioxygen, peroxide, superoxide,
9 any other form of active oxygen, nitrite, nitrate,
10 nitric acid or other oxides (or oxyhalides) of nitrogen
11 (hydrated or anhydrous) are preferably used as the
12 oxidising agent. The process is usually under Bronsted
13 acidic conditions.

14
15 Preferably, the process involves the oxidation of the
16 alkyl side chain of the aromatic compound in the
17 presence of a nitrogen oxyacid species such as nitrate
18 or nitric acid. This nitrogen(V) species oxidises the
19 alkyl group, and is in turn reduced to a lower valent
20 form of nitrogen. This lower valent form of nitrogen
21 can be re-oxidised back to nitrogen(V) by means of an
22 oxidising agent. Other oxidising agents suitable
23 include dioxygen (air), oxygen, peroxides, superoxides.

24
25 Other suitable oxidating agents are certain sulfur
26 compounds such as the sulfur acid/bases, eg H_2SO_4 or
27 H_2SO_3 .

28
29 This invention also allows for the separation of the
30 ionic liquid and product by physical or chemical means
31 such as distillation, steam distillation, azeotropic
32 distillation, sublimation, gravity separation, solvent

1 extraction, crystallisation, supercritical fluid
2 extraction and chromatography.

3
4 Ionic liquids consist of two components, which are a
5 positively charged cation and a negatively charged
6 anion. Generally, any compound that meets the
7 criterion of being a salt (consisting of an anion and
8 cation) and is fluid at or near the reaction
9 temperature or exists in a fluid state during any stage
10 of the reaction may be defined as an ionic liquid.

11
12 The cation for the present process is preferably a 1,
13 3-dialkylimidazolium cation such as 1-methyl-3-
14 butylimidazolium. Other cations for this process are
15 ammonium, pyrazolium, and other pyridinium, alkyl- or
16 poly-alkylpyridinium, alkyl- or poly-alkyl phosphonium
17 cations.

18
19 The anion for the process is preferably a sulfur-
20 containing anion, such as sulfate, hydrogensulfate.
21 Non-sulfur containing anions include those based on
22 nitrogen, phosphorus, boron, silicon, selenium,
23 tellurium, halogens, oxoanions of metals, and organic
24 anions, such as trifluoroacetate, acetate, and anions
25 that are arsenic, antimony, and bismuth based. The
26 preferred anions are nitrate or methanesulfonate.

27
28 More than one ionic liquid or any combination of ionic
29 liquids can be used in the present invention.
30 Suitable Process conditions.

31 Temperature: ideally 100-120°C but to include 0° to
32 250°C

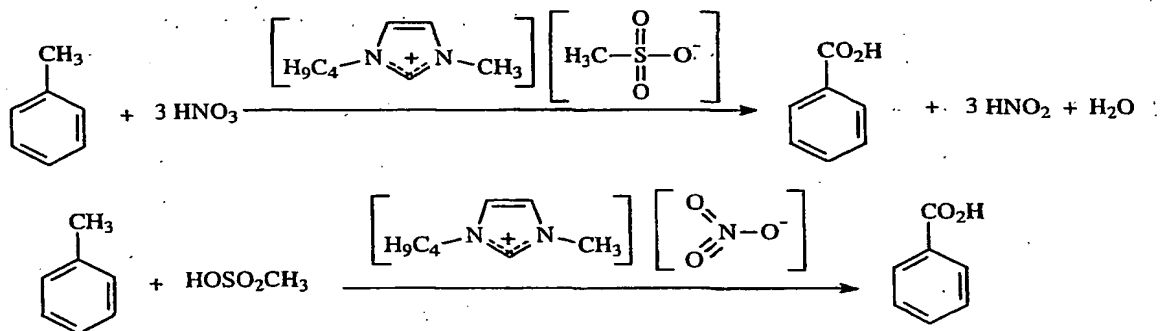
1 Pressure: ideally, atmospheric, but include 1 mbar
 2 to 100 bar
 3 Time: ideally 24-48 hours, can be 1 minute to
 4 1 month.

5
 6 The reaction preferably requires an acid to be present.
 7 This acid is generally an oxoacid of nitrogen, sulfur,
 8 selenium, tellurium, phosphorus, arsenic, antimony, or
 9 an organic acid anion (e.g. acetate, trifluoroacetate).

10

11 The oxidation of toluene is shown in scheme 1. As can
 12 be seen, the reaction can be carried out in [bmim][OMs]
 13 ("OMs" = methanesulfonate) by the addition of nitric
 14 acid or in [bmim][NO₃] by the addition of
 15 methanesulfonic acid.

16



20 Scheme 1. The oxidation of toluene to benzoic acid.

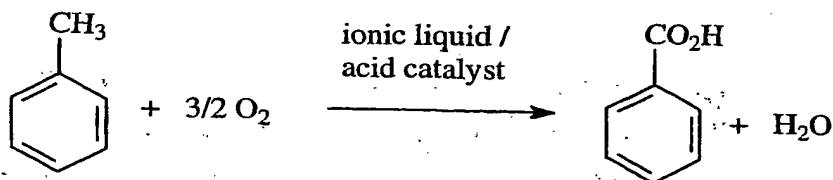
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22 As the reaction proceeds, the nitrate or nitric acid
 23 (the oxidising agent) is believed to be reduced to
 24 nitrous acid, which is
 25 unstable under the acidic conditions employed in the
 26 reaction. This in turn is re-oxidised back to
 27 nitrate/nitric acid by an oxidising agent. The

1 dioxygen in air will suffice, but other oxidants such
2 as peroxides are also suitable.

3

4 The reaction can be carried out using a stoichiometric
5 amount of nitric acid (or nitrate) or can be performed
6 catalytically. In the latter case, if air is used to
7 re-oxidise the nitrous acid formed in the reaction, the
8 overall reaction is shown in scheme 2.



12

13 Scheme 2: The overall reaction for the oxidation of
14 toluene in air.

15

16 Other compounds oxidizable by this invention are o- or
17 p-xylene, firstly to o- or p-toluic acid (2- or 4-
18 methylbenzoic acid) then to phthalic acid or
19 terphthalic acids respectively. Ethylbenzene and n-
20 propylbenzene can be oxidized under similar conditions
21 to acetophenone and propiophenone as the major
22 products. Also formed in these two reactions are
23 benzoic acid, presumably from oxidative cleavage of the
24 alkyl group.

25

26 The present invention is further illustrated with
27 reference to the following Examples:

1

2 Examples:

3

4 1. Oxidation of toluene in [bmim][OMs]

5 In a round-bottomed flask (25cm³) equipped with a
6 magnetic stirrer flea and reflux condenser, 1-butyl-
7 3-methylimidazolium methanesulfonate (0.23g, 1 mmol)
8 and toluene (0.18g, 2 mmol) were added. 67% aqueous
9 nitric acid (0.28g, 3 mmol) was cautiously added and
10 the mixture heated under reflux for 48 hours. The
11 flask was cooled and the products analysed by gas
12 chromatography. All of the toluene had reacted and
13 signals due to benzoic acid (70 % yield) and a by-
14 product (2- and 4-nitrotoluene) were detected. The
15 product(s) was isolated by Kugelrohr distillation at
16 5 mm Hg. This gave pale yellow oil (bp = 100°C at 5
17 mmHg) nitrotoluene and a colourless solid (bp = 150°C
18 at 5 mmHg) - benzoic acid. The structures were
19 confirmed by NMR analysis and were in accordance
20 with authentic material.

21

22

23 2. Oxidation of toluene in [bmim][OMs]

24 In a round-bottomed flask (25cm³) equipped with a
25 magnetic stirrer flea and reflux condensed, 1-butyl-
26 3-methylimidazolium methanesulfonate (0.23g, 1 mmol)
27 and toluene (0.46g, 5 mmol) were added. 67% aqueous
28 nitric acid (0.18g, 2 mmol) was cautiously added and
29 the mixture heated under reflux for 48 hours. The
30 flask was cooled and the products analysed by gas
31 chromatography. All of the toluene had reacted and
32 signals due to benzoic acid (90% yield) and a by-

1 product (2- and 4-nitrotoluene) were detected. The
2 product(s) was isolated by Kugelrohr distillation at
3 5 mmHg. This gave pale yellow oil (bp = 100°C at 5
4 mmHg) nitrotoluene and a colourless solid (bp = 150°
5 at 5 mmHg) - benzoic acid. The structures were
6 confirmed by NMR analysis and were in accordance
7 with authentic material.

8

9 3. Oxidation of toluene in [bmim][NO₃]

10 In a round-bottomed flask (25cm³) equipped with a
11 magnetic stirrer flea and reflux condensed, 1-butyl-
12 3-methylimidazolium nitrate (0.23g, 2 mmol) and
13 toluene (0.46g, 5 mmol) were added. 67%
14 methanesulfonic acid (0.29g, 3 mmol) was cautiously
15 added and the mixture heated under reflux for 48
16 hours. The flask was cooled and the products
17 analysed by gas chromatography. All of the toluene
18 had reacted and signals due to benzoic acid (85%
19 yield) and a by-product (2- and 4-nitrotoluene) were
20 detected. The product(s) was isolated by Kugelrohr
21 distillation at 5 mmHg. This gave pale yellow oil
22 (bp = 100°C at 5 mmHg) nitrotoluene and a colourless
23 solid (bp = 150° at 5 mmHg) - benzoic acid. The
24 structures were confirmed by NMR analysis and were
25 in accordance with authentic material.

26

27 4. Oxidation of ethylbenzene

28 In a 50 cm³ round bottomed flask, equipped with a
29 magnetic stirrer and reflux condenser, was added
30 ethylbenzene (1.06 g, 10 mmol) and [bmim][OMs] (1.0
31 g). 67 % Nitric acid (0.45 g, 5 mmol) was
32 cautiously added and the mixture heated under

1 reflux. After 48 hours the mixture was analysed by
2 gas chromatography and found to contain 19 %
3 unreacted ethylbenzene, 23 % benzoic acid and 57 %
4 acetophenone. The mixture was cooled and water (50
5 cm³) was added. The products were extracted with
6 diethyl ether (4 x 20 cm³), concentrated on a rotary
7 evaporator and purified by Kugelrohr distillation.
8 This gave acetophenone (0.62 g, 51 %) and benzoic
9 acid (0.22 g, 18 %).

10

11 5. Oxidation of *p*-xylene

12 In a 50 cm³ round bottomed flask, equipped with a
13 magnetic stirrer and reflux condenser, was added *p*-
14 xylene (1.07 g, 10 mmol) and [bmim][OMs] (2.0 g).
15 67 % Nitric acid (0.90 g, 10 mmol) was cautiously
16 added and the mixture heated under reflux. After 24
17 hours the mixture was analysed by gas chromatography
18 (approximately 50 % conversion), cooled and water
19 (50 cm³) was added. The resultant precipitate was
20 collected by filtration and purified by vacuum
21 sublimation on a Kugelrohr apparatus. This gave two
22 crystalline solids, that were identified as 4-
23 methylbenzoic acid (0.50 g, 37 %) and benzene-1,4-
24 dioic acid (terephthalic acid) (0.08 g, 5 %). The
25 remainder was unreacted *p*-xylene.

26

27 The aqueous filtrate containing the ionic liquid was
28 concentrated on a rotary evaporator (80°C at 50
29 mmHg) and transferred to the 50 cm³ round bottomed
30 flask, equipped with a magnetic stirrer and reflux
31 condenser. *p*-Xylene (5.35g, 50 mmol) and 67% nitric
32 acid (0.90 g, 10 mmol) was added. The mixture was

1 heated under reflux for 5 days, then cooled to room
2 temperature. During this time some of the *p*-xylene
3 was lost through evaporation. Dilution with water,
4 filtration and sublimation (as above) gave 4-
5 methylbenzoic acid (1.63 g, 24 %) and benzene-1,4-
6 dioic acid (terephthalic acid) (0.24 g, 3 %). The
7 remainder was unreacted *p*-xylene.

8

9 6. Oxidation of *o*-xylene

10 In a 50 cm³ round bottomed flask, equipped with a
11 magnetic stirrer and reflux condenser, was added *o*-
12 xylene (1.07 g, 10 mmol) and [bmim][OMs] (1.0 g).
13 67 % Nitric acid (0.45 g, 5 mmol) was cautiously
14 added and the mixture heated under reflux. After 40
15 hours the mixture was analysed by gas chromatography
16 and gave 42 % conversion to 2-methylbenzoic acid and
17 trace of phthalic acid. The remainder was unreacted
18 *o*-xylene.

19

20

21 7. Oxidation of propylbenzene

22

23 In a 50 cm³ round bottomed flask, equipped with a
24 magnetic stirrer and reflux condenser, was added
25 propylbenzene (1.21 g, 10 mmol) and [bmim][OMs] (1.0
26 g). 67 % Nitric acid (0.45 g, 5 mmol) was
27 cautiously added and the mixture heated under
28 reflux. After 54, 80 hours the mixture was analysed
29 by gas chromatography and found to give 15 %
30 conversion. Three products were identified (GCMS)
31 as: propiophenone, benzoic acid and 3-phenylpentane
32 in the ratio (2 : 1 : trace).

1 In particular, the present invention relates to a
2 process whereby aromatic compounds bearing an alkyl
3 substituent are oxidised on the alkyl chain on the
4 carbon atom next to the aromatic ring, and where the
5 oxidation is performed in an ionic liquid.

6
7 The product of the oxidation reaction is preferably
8 a carboxylic acid or ketone or an intermediate
9 compound in the oxidation such as an aldehyde, or
10 alcohol.

11
12 The oxidation is preferably performed in an ionic
13 liquid containing an acid promoter such as
14 methanesulfonic acid.

15
16 The oxidation is preferably performed in an ionic
17 liquid containing a nitrogen acid or salt such as
18 nitric acid, nitrous acid, nitrate or nitrite salt.
19 The ionic liquid/acidic promoter combination can be
20 used as a catalyst for the oxidation.

21
22 The ionic liquid/acidic promoter can be re-oxidised
23 by an oxidising agent (such as dioxygen in air), and
24 the ionic liquid/acidic promoter can be recycled and
25 reused in further reactions.

26
27 The ionic liquid/acidic promoter can be separated
28 from the product by some physical or chemical means
29 such as distillation, steam distillation, azeotropic
30 distillation, sublimation, gravity separation,
31 solvent extraction, crystallisation, supercritical
32 fluid extraction and chromatography.

1

2 The present invention also extends to the use of an
3 ionic liquid in the oxidation of an alkyl-aromatic
4 compound, as well as an oxidised alkyl-aromatic
5 compound whenever prepared by a process of the
6 present invention.

7

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9

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18

1 Claims

2

3 1. A process for the oxidation of an alkyl-
4 aromatic compound, wherein the aromatic
5 compound is admixed with an oxidising agent or
6 sulfur compound in the presence of an ionic
7 liquid.

8

9 2. A process as claimed in Claim 1 wherein the
10 oxidising agent is one or more of the group
11 comprising: air, dioxygen, peroxide,
12 superoxide, any other form of active oxygen,
13 nitrite, nitrate, nitric acid or other oxides
14 (or oxyhalides) of nitrogen (hydrated or
15 anhydrous) and sulfur acid/bases such as
16 sulfuric acid or sulfonic acid.

17

18 3. A process as claimed in Claim 1 or Claim 2
19 wherein the process is carried out under
20 Bronsted acidic conditions.

21

22 4. A process as claimed in any one of the
23 preceding Claims involving the oxidation of the
24 alkyl sidechain of the aromatic compound in the
25 presence of a nitrogen oxyacid species.

26

27 5. A process as claimed in Claim 4 wherein the
28 nitrogen oxyacid species is a nitrate or nitric
29 acid.

30

31 6. A process as claimed in any one of the
32 preceding Claims wherein the ionic liquid and

1 reaction products can be separated by means of
2 one or more of the following processes
3 comprising: distillation, steam distillation,
4 azeotropic distillation, sublimation, gravity
5 separation, solvent extraction,
6 crystallisation, supercritical fluid extraction
7 and chromatography.
8

9 7. A process as claimed in any one of the
10 preceding Claims wherein the cation of the
11 ionic liquid is one or more of the group
12 comprising: ammonium, pyrazolium, 1,3-
13 dialkylimidazolium, pyridinium, alkyl- or poly-
14 alkylpyridinium, alkyl- or poly-alkyl
15 phosphonium.
16

17 8. A process as claimed in Claim 7 wherein cation
18 is a 1, 3-dialkylimidazolium cation such as 1-
19 methyl-3-butyylimidazolium.
20

21 9. A process as claimed in any one of the
22 preceding Claims wherein the anion of the ionic
23 liquid is one or more of the group comprising:
24 a sulfur-containing anion, such as sulfate,
25 hydrogensulfate, non-sulfur-containing anions
26 including those based on nitrogen, phosphorus,
27 boron, silicon, selenium, tellurium, halogens,
28 oxoanions of metals, and organic anions, such
29 as trifluoroacetate, acetate, and anions that
30 are arsenic, antimony, and bismuth-based.
31

- 1 10. A process as claimed in Claim 9 wherein the
2 anion is nitrate or methanesulfonate.
3
- 4 11. A process as claimed in any one of the
5 preceding Claims wherein more than one ionic
6 liquid or any combination of ionic liquids is
7 used.
8
- 9 12. A process as claimed in any one of the
10 preceding Claims wherein an acid is present.
11
- 12 13. A process as claimed in Claim 12 wherein the
13 acid is one or more of the group comprising: an
14 oxoacid of nitrogen, sulfur, selenium,
15 tellurium, phosphorus, arsenic, antimony, or an
16 organic acid anion (e.g. acetate or
17 trifluoroacetate).
18
- 19 14. A process as claimed in claim 13 wherein the
20 acid is one or more of the following group
21 comprising: methanesulfonic acid, nitric acid,
22 nitrous acid, nitrate or a nitrate salt.
23
- 24 15. A process as claimed in any one of Claims 12 to
25 14 wherein the ionic liquid/acid combination
26 also acts as a catalyst for the oxidation.
27
- 28 16. A process as claimed in any one of Claims 12 to
29 15 wherein the acid can be re-oxidised by an
30 oxidising agent such as dioxygen in air.
31

- 1 17. A process as claimed in any one the preceding
2 Claims wherein the ionic liquid is [bmin] [OMs]
3 and the oxidising agent is nitric acid.
4
- 5 18. A process as claimed in any one of Claims 1 to
6 16 wherein the ionic liquid is [bmin] [NO₃] and
7 the oxidising agent is methanesulfonic acid.
8
- 9 19. A process as claimed in any one of the
10 preceding Claims for the oxidation of
11 alkylaromatics, toluene, xylene, or a benzene.
12
- 13 20. A process as claimed in Claim 19 for the
14 oxidation of p-xylene.
15
- 16 21. A process as claimed in any one of the
17 preceding Claims wherein the alkyl chain on the
18 carbon atom next to the aromatic ring is
19 oxidised.
20
- 21 22. A process as claimed in any one of the
22 preceding Claims for the preparation of an
23 aldehyde or alcohol.
24
- 25 23. Use of an ionic liquid in a process as claimed
26 in any one of Claims 1 to 22.
27
- 28 24. Use of an ionic liquid in the oxidation of
29 alkylaromatics, toluene, xylene or a benzene.
30

- 1 25. An oxidated alkyl-aromatic compound obtainable
2 by a process as defined in any one of Claims 1
3 to 22.
4
- 5 26. A compound as claimed in Claim 25 wherein the
6 alkyl aromatic starting compound is an
7 alkylaromatic, toluene, xylene or a benzene.
8
- 9 27. A process substantially as hereindescribed and
10 with reference to the Examples.

INTERNATIONAL SEARCH REPORT

Int ional Application No

PCT/GB 01/04426

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C51/265

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 199 01 524 A (WAFFENSCHMIDT HORST ; KEIM WILHELM (DE); WASSERSCHIED PETER (DE)) 20 July 2000 (2000-07-20) example 5	1-27
X	WO 00 32572 A (MURPHY VINCE ; HAGEMEYER ALFRED (US); POOJARY DAMODARA M (US); SYM) 8 June 2000 (2000-06-08) page 25, line 16,26	1-27

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☒ Patent family members are listed in annex.

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NL - 2280 HV Rijswijk
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19901524	A	20-07-2000	DE	19901524 A1	20-07-2000
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